CLAIMS

What is claimed is:

1. A recombinant adenovirus comprising:

an HIV sequence encoding an HIV antigen, expression of the HIV antigen by the recombinant adenovirus eliciting an immune response directed against the HIV antigen in a host upon infection of the host by the recombinant adenovirus.

2. The recombinant adenovirus of claim 1, wherein the recombinant adenovirus is replication-incompetent.

3. The recombinant adenovirus of claim 1, wherein the HIV antigen is an antigen of HIV-1 or HIV-2.

4. The recombinant adenovirus of claim 1, wherein the HIV antigen is an antigen of HIV strain BH10 or pNL4-3.

5. The recombinant adenovirus of claim 1, wherein the HIV antigen is an antigen of HIV clade A, B, C, D, E, F, or G.

6. The recombinant adenovirus of claim 1, wherein the HIV antigen is an HIV glycoprotein or surface antigen.

7. The recombinant adenovirus of claim 6, wherein the HIV glycoprotein is an HIV envelope protein.

8. The recombinant adenovirus of claim 7, wherein the HIV envelope protein is a wild type or mutant gp160, gp120, or gp41.

9. The recombinant adenovirus of claim 7, wherein the cleavage site of the HIV envelope protein is inactivated by mutation.

10. The recombinant adenovirus of claim 7, wherein the C-terminal cytosolic domain of the HIV envelope protein is deleted.

11. The recombinant adenovirus of claim 7, wherein both the cleavage site and the C-terminal cytosolic domain of the HIV envelope protein are deleted.

12. The recombinant adenovirus of claim 7, wherein the HIV envelop protein is encoded by a polynucleotide selected from the group consisting of SEQ ID NOs: 14, 16, 20, 21, 22, 23, and 24.

13. The recombinant adenovirus of claim 7, wherein the HIV sequence further encodes an HIV regulatory protein selected from the group consisting of Tat, Vif, Nef, and Rev.

14. The recombinant adenovirus of claim 7, wherein the HIV antigen is a modified HIV envelope protein that includes multiclade variable loops.

15. The recombinant adenovirus of claim 14, wherein the multiclade variable loops are V3 loops from at least two HIV clades.

16. The recombinant adenovirus of claim 15, wherein the at least two HIV clades are selected from the group consisting of clade A, B, C, D, E, F, and G of group M of HIV-1 isolates.

17. The recombinant adenovirus of claim 15, wherein the V3 loops are encoded by polynucleotides selected from the group consisting of SEQ ID NOs: 25, 26, 27, 28, 29, 30, and 31.

18. The recombinant adenovirus of claim 14, wherein the modified HIV envelope protein that includes multiclade variable loops is encoded by a polynucleotide selected from the group consisting of SEQ ID NOs: 32, 52, and 54.

19. The recombinant adenovirus of claim 1, further comprising:

a polynucleotide encoding a signal peptide that facilitates the secretion of the HIV antigen by a cell infected by the recombinant adenoviruse.

20. The recombinant adenovirus of claim 19, wherein the signal peptide is an HIV gp120 signal peptide.

21. The recombinant adenovirus of claim 19, wherein the signal peptide is encoded by SEQ ID NO: 74.

22. The recombinant adenovirus of claim 1, further comprising:

a polynucleotide encoding an membrane-anchoring domain that renders the HIV antigen bound to the surface of a cell infected by the recombinant adenoviruse.

23. The recombinant adenovirus of claim 22, wherein the membrane-anchoring domain is an HIV gp41 transmembrane domain.

24. The recombinant adenovirus of claim 22, wherein the membrane-anchoring domain is encoded by SEQ ID NO: 75.

25. The recombinant adenovirus of claim 1, wherein the HIV antigen is an HIV structural protein.

26. The recombinant adenovirus of claim 25, wherein the HIV structural protein is a wild type HIV Gag.

27. The recombinant adenovirus of claim 25, wherein the HIV structural protein is a proteolytic fragment of HIV Gag.

28. The recombinant adenovirus of claim 27, wherein the proteolytic fragment of HIV Gag is selected from the group consisting of p17/24, p17 and p24.

29. The recombinant adenovirus of claim 27, wherein the proteolytic fragment of HIV Gag is in a natural, secreted or membrane bound form.

30. The recombinant adenovirus of claim 27, wherein the proteolytic fragment of Gag is encoded by a polynucleotide selected from the group consisting of SEQ ID NOs: 34, 35, 36, 40, 41, 42, 46, 47, and 48.

31. The recombinant adenovirus of claim 1, further comprising:
a polynucleotide encoding an HIV protease.

32. The recombinant adenovirus of claim 31, wherein the polynucleotide encoding an HIV protease is SEQ ID NO: 56.

33. The recombinant adenovirus of claim 31, wherein the HIV antigen is HIV Gag.

34. The recombinant adenovirus of claim 33, wherein the protease is expressed as a fusion protein with the HIV Gag.

35. The recombinant adenovirus of claim 33, wherein the protease is expressed separately from a promoter different from that for the HIV Gag.

36. The recombinant adenovirus of claim 33, wherein the protease is expressed as a separate protein from the same promoter for the HIV Gag via an IRES or splicing donor/acceptor mechanism.

37. The recombinant adenovirus of claim 1, further comprising:

an immuno-stimulator sequence heterologous to adenovirus and encoding an immuno-stimulator whose expression in the host enhances the immunogenicity of the HIV antigen.

38. The recombinant adenovirus of claim 37, wherein the HIV sequence is positioned in the E1 region of the adenovirus and the immuno-stimulator sequence is positioned in the E4 region of the adenovirus.

39. The recombinant adenovirus of claim 37, wherein both the HIV sequence and the immuno-stimulator sequence are positioned in the E1 or E4 region of the adenovirus, and are expressed from the same promoter bicistronically via an internal ribosomal entry site or via a splicing donor-acceptor mechanism.

40. The recombinant adenovirus of claim 37, wherein the expression of the HIV antigen or the immuno-stimulator is controlled by an adenoviral promoter.

41. The recombinant adenovirus of claim 37, wherein the expression of the HIV antigen or the immuno-stimulator is controlled by a non-adenoviral promoter.

42. The recombinant adenovirus of claim 41, wherein the non-adenoviral promoter is selected from the group consisting of CMV promoter, SV40 promoter, retrovirus LTR promoter, and chicken cytoplasmic β-actin promoter.

43. The recombinant adenovirus of claim 37, wherein the immuno-stimulator is a cytokine.

44. The recombinant adenovirus of claim 43, wherein the cytokine is selected from the group consisting of interleukin-2, interleukin-4, interleukin-12, β- interferon, λ-interferon, γ-interferon, granulocyte colony stimulating factor, and granulocyte-macrophage colony stimulating factor.

45. The recombinant adenovirus of claim 37, wherein the immuno-stimulator is a combination of different cytokines.

46. The recombinant adenovirus of claim 45, wherein the combination of cytokines are expressed from the same promoter but as separate proteins via an IRES mechanism or a retroviral splicing donor/acceptor mechanism.

47. A recombinant adenovirus comprising:

a first HIV sequence encoding a first HIV antigen, expression of which is under the transcriptional control of a first promoter; and

a second HIV sequence encoding a second HIV antigen, expression of which is under the transcriptional control of a second promoter positioned in a different region than the first promoter,

expression of the first and second HIV sequences eliciting an immune response directed against the first and second HIV antigens upon infection of the host by the recombinant virus.

48. The recombinant adenovirus of claim 47, wherein the recombinant adenovirus is replication-incompetent.

49. The recombinant adenovirus of claim 47, wherein the first and second HIV antigens are the same.

50. The recombinant adenovirus of claim 47, wherein the first and second HIV antigens are different.

51. The recombinant adenovirus of claim 47, wherein the first or second HIV antigen is an HIV envelope protein.

52. The recombinant adenovirus of claim 51, wherein the HIV envelope protein is a wild type or mutant gp160, gp120, or gp41.

53. The recombinant adenovirus of claim 52, wherein the cleavage site of the HIV envelope protein is inactivated by mutation.

54. The recombinant adenovirus of claim 52, wherein the C-terminal cytosolic domain of the HIV envelope protein is deleted.

55. The recombinant adenovirus of claim 52, wherein both the cleavage site and the C-terminal cytosolic domain of the HIV envelope protein are deleted.

56. The recombinant adenovirus of claim 51, wherein the first or second HIV sequence further encodes an HIV regulatory protein selected from the group consisting of Tat, Vif, Nef, and Rev.

57. The recombinant adenovirus of claim 47, wherein the first or second HIV antigen is a modified HIV envelope protein that includes multiclade variable loops.

58. The recombinant adenovirus of claim 57, wherein the multiclade variable loops are V3 loops from at least two HIV clades.

59. The recombinant adenovirus of claim 58, wherein the at least two HIV clades are selected from the group consisting of clade A, B, C, D, E, F, and G of group M of HIV-1 isolates.

60. The recombinant adenovirus of claim 58, wherein the V3 loops are encoded by polynucleotides selected from the group consisting of SEQ ID NOs: 25, 26, 27, 28, 29, 30, and 31.

61. The recombinant adenovirus of claim 47, further comprising:

a polynucleotide encoding a signal peptide that facilitates the secretion of the first or second HIV antigen by a cell infected by the recombinant adenoviruse.

62. The recombinant adenovirus of claim 61, wherein the signal peptide is an HIV gp120 signal peptide.

63. The recombinant adenovirus of claim 61, wherein the signal peptide is encoded by SEQ ID NO: 74.

64. The recombinant adenovirus of claim 47, further comprising:

a polynucleotide encoding an membrane-anchoring domain that renders the first or second HIV antigen bound to the surface of a cell infected by the recombinant adenoviruse.

65. The recombinant adenovirus of claim 64, wherein the membrane-anchoring domain is an HIV gp41 transmembrane domain.

66. The recombinant adenovirus of claim 64, wherein the membrane-anchoring domain is encoded by SEQ ID NO: 75.

67. The recombinant adenovirus of claim 47, wherein the first and second HIV antigen is an HIV structural protein.

68. The recombinant adenovirus of claim 67, wherein the HIV structural protein is a wild type HIV Gag.

69. The recombinant adenovirus of claim 67, wherein the HIV structural protein is a proteolytic fragment of HIV Gag.

70. The recombinant adenovirus of claim 67, wherein the proteolytic fragment of HIV Gag is selected from the group consisting of p17/24, p17 and p24.

71. The recombinant adenovirus of claim 67, wherein the proteolytic fragment of HIV Gag is in a natural, secreted or membrane bound form.

72. The recombinant adenovirus of claim 67, wherein the proteolytic fragment of Gag is encoded by a polynucleotide selected from the group consisting of SEQ ID NOs: 34, 35, 36, 40, 41, 42, 46, 47, and 48.

73. The recombinant adenovirus of claim 67, further comprising:
a polynucleotide encoding an HIV protease.

74. The recombinant adenovirus of claim 73, wherein the polynucleotide encoding an HIV protease is SEQ ID NO: 56.

75. The recombinant adenovirus of claim 47, wherein the first HIV antigen is a wildtype or mutant HIV envelope protein, and the second HIV antigen is a wildtype or mutant HIV structural protein.

76. The recombinant adenovirus of claim 75, wherein wildtype or mutant HIV structural protein is wildtype Gag or a proteolytic fragment of Gag.

77. The recombinant adenovirus of claim 47, wherein both the first and second HIV antigen are a wildtype or mutant HIV envelope protein.

78. The recombinant adenovirus of claim 47. wherein both the first and second HIV antigen are a wildtype or mutant HIV structural protein.

79. The recombinant adenovirus of claim 47, further comprising:
an immuno-stimulator sequence heterologous to adenovirus and encoding an immuno-stimulator whose expression in the host enhances the immunogenicity of the first or second HIV antigen.

80. The recombinant adenovirus of claim 79, wherein the first or second HIV sequence and the immuno-stimulator sequence are expressed from the same promoter bicistronically via an internal ribosomal entry site or via a splicing donor-acceptor mechanism.

81. The recombinant adenovirus of claim 79, wherein the immuno-stimulator is a cytokine.

82. The recombinant adenovirus of claim 81, wherein the cytokine is selected from the group consisting of interleukin-2, interleukin-4, interleukin-12, β- interferon, λ-interferon, γ-interferon, granulocyte colony stimulating factor, and granulocyte-macrophage colony stimulating factor.

83. The recombinant adenovirus of claim 47, wherein the first or second promoter is an adenoviral promoter.

84. The recombinant adenovirus of claim 47, wherein the first or second promoter is non-adenoviral promoter.

85. The recombinant adenovirus of claim 84, wherein the non-adenoviral promoter is selected from the group consisting of CMV promoter, SV40 promoter, retrovirus LTR promoter, and chicken cytoplasmic β-actin promoter.

86. The recombinant adenovirus of claim 47, wherein the first promoter is in the E1 region of the adenovirus and the second promoter is positioned in the E4 region of the adenovirus.

87. A method for enhancing the immunity of a host to HIV infection, comprising:

administering to the host a recombinant adenovirus comprising an HIV sequence encoding an HIV antigen, expression of the HIV antigen by the recombinant adenovirus eliciting an immune response directed against the HIV antigen in a host upon infection of the host by the recombinant adenovirus.

88. The method of claim 87, wherein administering to the host a recombinant adenovirus is performed intramuscularly, intratracheally, subcutaneously, intranasally, intradermally, rectally, orally or parentally.

89. The method of claim 87, wherein the recombinant adenovirus further comprises one or more immuno-stimulator sequences heterologous to adenovirus that encodes an immuno-stimulator whose expression in the host enhances the immunogenicity of the HIV antigen.

90. The method of claim 87, further comprising:
administering to the host an immuno-stimulator.

91. The method of claim 90, wherein the immuno-stimulator is a cytokine selected from the group consisting of interleukin-2, interleukin-4, interleukin-12, β- interferon, λ-interferon, γ-interferon, granulocyte colony stimulating factor, and granulocyte-macrophage colony stimulating factor.

92. A method of enhancing the immunity of a host to HIV infection, comprising:

administering to the host a recombinant adenovirus comprising

a first HIV sequence encoding a first HIV antigen, expression of which is under the transcriptional control of a first promoter; and

a second HIV sequence encoding a second HIV antigen, expression of which is under the transcriptional control of a second promoter positioned in a different region than the first promoter,

expression of the first and second HIV sequences eliciting an immune response directed against the first and second HIV antigens upon infection of the host by the recombinant virus.

93. The method of claim 92, further comprising:

administering to the host the recombinant adenovirus at least once again after the initial administration of the recombinant adenovirus.